

REMARKS

The Examiner has objected to the specification on the basis that terminology of Liquid-Liquid-Liquid is not clear and specifically on page 8, third paragraph wherein the phrase “the solvent forming membrane” is not clear.

The Applicants have amended the specification in order to clarify that the second liquid is a membrane itself and is filled in and supported by a hollow fibre.

The terminology “filling” is supported by the specification on page 10, last line. The term “supported” is found in the Figure 3b. Figure 3a shows the hollow fibre and Figure 3 shows the liquid membrane impermeated in, or filled in and supported by the hollow fibre. The Applicant respectfully submits that this clarifies the liquids utilized in liquid-liquid-liquid micro extraction method also referred to in the specification as LLLME.

Claims 42-47 has been rejected by the Examiner under 35 USC 103(a) as being unpatentable over U.S. 3,429,785 to Ross in view of U.S. 3,647,666 to Simon, et al.

In this rejection, the Examiner states that Ross describes a method comprising the steps:

(1) providing a first container (see Figure 6, container comprising test solution 72) having a sample solution (see Figure 6, test solution 72) comprising a dissolved analyte (see Abstract, “ionic species”);

(2) providing a second container (see e.g., Figure 1, ion sensitive electrode 20) with a membrane wall (see e.g., Figure 1, membrane 22) having fiber pores (see e.g., column 5, lines 17-18, “porous polyethylene”);

(3) filling the second container with an acceptor solution (see e.g., Figure 1, ion exchanger liquid 24);

(4) lowering the second container into the first container (see Figure 6, container comprising ion sensitive electrode 50); and

(5) stirring the sample solution (see column 8, lines 8-9, “[s]steady state conditions of potential were established”);

The Examiner acknowledges that does not teach a removing analyte enriched acceptor solution from the second container. Therefore, the Examiner reaches to Simon, et al. for describing an electrode design having a detachable base (see Fig. 1, electrode base 10) for removing acceptor solutions (see column 4, lines 2-3, “exchange of the reference solution”) from the electrode.

The Examiner then concludes it would have been obvious to persons of ordinary skill to perform Ross’ method with Simon’s electrode design because Simon says his design allows for easy and rapid replacement of ion-exchange membranes and acceptor impregnates.

The Examiner also states that Simon, et al. describes the claimed “stirring” step (see column 2, line 26, “agitated”).

The Applicants submit that the Examiner has not made a *prima facie* case of obviousness under 35 USC 103(a) on the basis of Ross and Simon, et al. references.

Ross teaches organic liquid ion-exchange electrode. Figure 6 relied on by the Examiner is directed to a water-hardness and tester utilizing ion sensing electrode 50 and reference electrode 56 disposed in a test solution.

There is, of course, no suggestion of stirring the sample solutions since the operation of the apparatus is by electrolysis. In addition, there is no equilibrium established between the analyte and the sample solution and the analyte in the acceptor solution by passing of analyte through a membrane wall as presently claimed. In fact, Figure 6 of Ross shows only one test solution.

The present invention is not an electrolysis cell. No electrical power is provided for the micro-extraction method presently claimed. In fact, Ross and Simon, et al. are both directed to electrode cells. Accordingly, they both represent non-analogous art and are not suitable references for establishing a *prima facie* case of obviousness.

In fact, Simon et al describes a totally different invention than covered in the subject patent application, namely an electrode device for the potentiometric measurements of different ions in solution. Thus, in the reference by Simon et al, concentrations of a particular ion in an aqueous sample solution is measured directly by the electrical potential difference arising between a reference electrode and an ion-selective electrode which both are placed in said sample. The novelty of the reference of Simon et al is that the reference electrode and the ion-selective electrode are incorporated in the same device and that the ion-selective part of the electrode is easily changed to facilitate measurement of different ions. It obviously represented an advance in the field of electro-analytical chemistry

In contrast, the present application describes a micro extraction method for a broad range of chemical substances, where said substances are extracted from aqueous samples, through a liquid membrane sustained in the pores of a porous hollow fiber, and into an acceptor solution placed inside the lumen of the hollow fiber. After this extraction, the acceptor solution is transferred to a final chemical analysis by chromatography, electrophoresis, or mass spectrometry, which serves to determine each substance individually. Thus, the present application describes a pre-analysis device capable for the simultaneous determination of a broad range of chemical substance simultaneously, whereas the reference of Simon et al describes an analysis device for single ions. The present application obviously describes an advance in the field of sample preparation for chromatography, electrophoresis, and mass spectrometry.

In the reference of Simon et al, a semi-permeable membrane is included in the device which allows the particular type of ion to pass, whereas all other ions in principle are prevented from diffusion through the membrane. The analytical signal is gained by this diffusion of the particular ion from the sample solution, across the semi-permeable membrane, and into an

internal solution on the other side. The reference of Simon is vague on compositional information about the semi-permeable membrane, but it is clear that it is composed by an ion-selective liquid immobilized in the pores of a solid support. However, it is generally known to people skilled in analytical chemistry that the ion-selective liquid membranes in use consist of conducting liquids having ion-exchanger properties. Thus, it is electrically conducting to ensure electrical contact over the system and to give the analytical response, and it has ion-exchange properties to selectively bond the ions of interest. This is totally different to the characteristics and the function of the supported liquid membrane described in the present application. Thus, in the present application the membrane is a non-conducting organic solvent as the system involves no measurement of electrical potentials, and it has no ion-exchange properties as ion-exchange is not involved in the extraction principle at all. The purpose of the liquid membrane in the present application is only to dissolve chemical substances in their neutral form intermediately as they are extracted from the sample solution and into the acceptor solution, and to physically separate the sample and the acceptor solution. Thus, the mechanisms are totally different, and as so, it is clearly not obvious for a person skilled in analytical chemistry to develop the membrane of the present application based on the reference of Simon et al.

Two criteria have evolved for determining whether prior art is analogous:

- (1) Whether the art is from the same field of endeavor, regardless of problem address and
- (2) if the reference is not within the field of the inventors' endeavor, whether the reference is still reasonably pertinent to the particular problem from which the inventors are involved. *In re Deminski*, 230 USPQ 313, 315 (Fed. Cir. 1986); *In re Wood*, 202 USPQ 171, 174 (CCPA 1979).

The Ross and Simon, et al. art is not relevant because one skilled in the art would not reasonably be expected to look at the electrolysis equipment in order to solve the problem of micro-extraction.

Utilizing the hereinabove set forth criteria is clear that the prior art is not from the same field of endeavor. Both Ross and Simon, et al. are directed to measurement of the concentration

of ionic species in solution and also methods for determining activity or concentration of ionic species and novel apparatus for using in such determination.

On the other hand, the present invention is directed to an extraction method, specifically a micro-extraction method in which analytes are extracted from a large volume of sample solution into a small body of an acceptor phase. One must conclude that this field of endeavor is entirely different than that of Ross and Simon, et al.

Second, in the criteria hereinabove set forth, is the step of establishing whether Ross and Simon, et al. are reasonably pertinent to the particular problem from which the inventor is involved.

Clearly, the answer to that must also be no since Ross and Simon, et al. are directed to measurement of the concentration of ionic species in solution of the present invention is directed to the extraction of analytes from a large volume of sample, as hereinabove noted.

Since Ross and Simon, et al. are not in the same field of endeavor and not pertinent to a particular problem with which the inventor is involved, they must be considered non-analogous art and accordingly not suitable references for reliance in determining a *prima facie* case of obviousness under 35 USC 103(a).

Accordingly, the Applicants submit that there is “no apparent reason” to combine the references or modify the prior art to create the allegedly obvious invention in accordance with *KSR International v. Teleflex, Inc.*, 82 USPQ 2d 1385 (U.S. 2007).

In view of the arguments hereinabove set forth and amendment to the specification, it is submitted that each of the claims now in the application define patentable subject matter not anticipated by the art of record and not obvious to one skilled in this field who is aware of the references of record. Reconsideration and allowance are respectfully requested.

Also enclosed is an Information Disclosure Statement referencing U.S. 5,277,821 to Coughlin and a Petition for Consideration.

The Applicant also respectfully request is that all future correspondence be directed to:

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